

Minocycline hydrochloride (Minocin) as a single-dose oral treatment of uncomplicated gonorrhoea in men

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Summary

349 male patients with uncomplicated gonococcal urethritis were treated with a single dose of 300 mg. or 400 mg. minocycline hydrochloride.

The lower dose gave a lower failure rate, 3.2 compared with 5.1 per cent., but this difference was not statistically significant. The overall known failure rate of 4.2 per cent. compares most favourably with our previous findings in this area using other drugs of the tetracycline group. The incidence of post-gonococcal urethritis (5.1 per cent.) was also the lowest we have found. The few side-effects reported were comparatively trivial.

Because of its high degree of therapeutic efficacy, the relative lack of side-effects, and the reduced incidence of post-gonococcal urethritis, minocycline hydrochloride should be considered the drug of choice whenever single-dose oral treatment is given in uncomplicated gonorrhoea in men.

Introduction

The increasing relative resistance of gonococci to penicillin has meant that over the years the dose has had to be increased at regular intervals to remain effective. Some centres have already used as much as 5 m.u. penicillin with probenecid to treat gonorrhoea (Gray, Phillips, and Nicol, 1970). This is thirty times the amount of the crude penicillin which gave satisfactory cure rates in the early 1940s.

Phillips, Rimmer, Ridley, Lynn, and Warren (1970) pointed out that the dose of penicillin could not be increased indefinitely in this fashion and urged that the search for alternatives should continue.

Sharing this opinion, we have concentrated upon the tetracycline groups as no relative resistance to them has been noted among the strains of gonococci isolated locally (Laidlaw, 1973). Several broad-spectrum antibiotics have been evaluated in this department (Masterton and Schofield, 1972; Masterton, Scho-

field, and Tait, 1973; Schofield and Masterton 1974); the failure rates have been acceptably low, but side-effects have sometimes been troublesome.

Minocin (minocycline hydrochloride) is a new semi-synthetic tetracycline which has been the subject of several investigations. Duncan, Glicksman, Knox, and Holder (1971) compared minocycline with tetracycline against strains of *Neisseria gonorrhoeae*. The minimum inhibitory concentrations (MIC) of minocycline and tetracycline were in the same general range (median MIC of 0.5 µg./ml. for each). In clinical trials of minocycline so far carried out, failure rates in gonococcal urethritis have varied from 25 per cent. (Duncan and others, 1971) to 4.5 per cent. (Thatcher, Pazin, and Domesick, 1970).

The present study compares the efficacy of two single-dose schedules in the treatment of uncomplicated gonorrhoea in men. The design of the trial was identical with that of our previous studies of broad-spectrum antibiotics.

Material and methods

349 male patients with uncomplicated gonococcal urethritis were treated with minocycline hydrochloride, alternate patients being given either three tablets (300 mg.) or four tablets (400 mg.) in a single dose. Patients with complicated infections, known previous defaulters, and those in transit were excluded from the study.

Of the 349 men suffering from uncomplicated gonorrhoea, 95 (27 per cent.) were married and 254 (73 per cent.) were born in the United Kingdom; 36 (10 per cent.) were teenagers and a further 159 (46 per cent.) were under 30 years of age.

A presumptive diagnosis of gonorrhoea was made by examining Gram-stained smears of urethral exudate. The diagnosis was confirmed by culture, and the MIC of penicillin G for each strain was determined, and also its sensitivity or resistance to tetracycline, streptomycin, kanamycin, and sulphafurazole (Table I).

Similar laboratory investigations to those described above were adopted for all patients with post-treatment urethritis.

The tablets were given with a drink of water under supervision in the clinic. It was planned to re-examine the patients on day 2, 4/5, 8, 15, and 29 after treatment.

TABLE I *Initial sensitivities of infecting gonococci*

MIC ($\mu\text{g./ml.}$) of penicillin G	Strains		Number of strains resistant to:	
	No.	Per cent.	Streptomycin	Sulphafurazole
0.03	269	77.1	16	0
0.06	44	12.6	12	0
0.15	20	5.7	6	7
0.3	8	2.3	1	3
0.6	6	1.7	5	4
1.2	2	0.6	1	1
Total	349	100.0	41 (11.7 per cent.)	15 (4.3 per cent.)

N.B. No strain was resistant to tetracycline or kanamycin.

TABLE II *Cumulative results*

Day	No. on surveillance	Last attendance	Reason for withdrawal from trial			
			Subsequent default	Post-treatment NSU	Re-infection	Treatment failure
1	349	21	21	0	0	0
2	328	47	38	6	0	3
4/5	281	35	24	4	0	7
8	246	17	6	6	2	3
15	229	9	2	0	7	0
22	220	4	2	0	2	0
29	216	216	0	0	0	0
Total		349	93	16	11	13

Results

Because of erratic attendance, the routine examination planned for the month after treatment was not always possible; 21 (6 per cent.) of the patients failed to return after treatment, 68 more defaulted within the first 2 weeks, and four during the second fortnight. However, 216 (62 per cent.) did complete the 4 weeks' surveillance satisfactorily (Table II).

Of the 328 patients who returned after treatment, sixteen (5.1 per cent.) had, or developed, non-specific urethritis. Of the remainder, 24 (7.7 per cent.) still had, or developed, a gonococcal urethritis after treatment. As with the initial infections, gonococci were identified by microscopy but the findings were always confirmed by culture. Eleven (3.5 per cent.) of these patients were considered to have been re-infected because of admitted re-exposure to risk of infection and a significant alteration in the anti-biogram. The remaining thirteen (4.2 per cent.) were regarded as treatment failures because they denied re-exposure to risk and the second anti-

biogram was similar to the original one. The results of the two treatment schedules are compared in Table III. Although there is a lower failure rate among those given 300 mg. Minocin (3.2 per cent.) than in those given 400 mg. (5.1 per cent.), the difference did not reach statistical significance ($\chi^2=0.72$; $0.4 > P > 0.3$).

Side-effects were minimal and insignificant. Five (1.5 per cent.) of the 328 patients who returned after treatment had complaints, two of dizziness and three of nausea. No patient complained of vomiting or diarrhoea.

Of the 349 strains of gonococci, 36 (10.3 per cent.) required an MIC of penicillin G in excess of 0.1 $\mu\text{g./ml.}$ No strain was resistant to tetracycline or kanamycin.

Discussion

The known treatment failure rate in uncomplicated gonorrhoea in this trial was 4.2 per cent., the lowest

TABLE III *Analysis of the two treatment schedules*

Dosage of minocycline hydrochloride (mg.)	Total treated	Number followed-up	Post-treatment NSU	Re-infected	Treatment failures	
					No.	Per cent.
300	173	164	8	6	5	3.2
400	176	164	8	5	8	5.1

TABLE IV Comparison of results of several single-dose oral treatments of uncomplicated gonorrhoea in men

Year	Drug	Dosage	No. of patients	Known failure rate (per cent.)	Post-treatment NSU (per cent.)	Side-effects (per cent.)
1969/70	Vibramycin (capsules)	300 mg.	107	6.4	7.8	3.5 ^a
1970	Deteclo (tablets)	1.2 to 2.4g	220	7.1	9.8	16.0 ^b
1972/73	Vibramycin (syrup)	300 mg.	144	6.9	5.8	2.0
1974	Minocin (tablets)	300 or 400 mg.	349	4.2	5.1	1.5

^aTaken with milk^bUsing metaclopramide monohydrate (5 mg.) as an antiemetic

we have obtained in any similar trial to date. There was no apparent clinical advantage in giving four tablets rather than three, the results being similar. Because we invariably follow the same criteria in all drug trials, it is possible to compare the results of this one with those carried out previously (Table IV). The failure rate was the lowest we have obtained, as was the incidence of post-treatment non-specific urethritis (5.1 per cent.) and of side-effects (1.5 per cent.).

The comparative absence of side-effects was particularly impressive. It is conceivable that a few patients, gratified by the rapid disappearance of symptoms, may have ignored minor upsets after therapy, but such magnanimity is not a characteristic of the local patients. It is firmly believed that minocycline hydrochloride, used in single doses as described, produces relatively few minor side-effects and is very effective therapeutically.

Minocycline hydrochloride was not included in the sensitivity tests, but Steigbigel, Reed, and Finland (1968) and Duncan and others (1971) have

shown that the sensitivity of the gonococcus to this drug is similar to tetracycline.

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